





THE following is a record of the past year's more obvious accomplishments. It is hoped and believed, however, that the net effect of the Howe Laboratory is considerably more than the sum of the projects herein described. It is even possible that the greatest benefit may ultimately be derived from some of the many activities that at the moment do not appear particularly newsworthy and are accordingly not here included.

## GLAUCOMA

For as long as glaucoma has been recognized as a clinical entity, it has been a subject of continual study. Its tremendous practical importance as a leading cause of blindness has resulted in the development of surgical and pharmacologic techniques to an advanced degree. But the real challenge from the research point of view stems from the evidence suggesting that glaucoma is basically an alteration of the normal intra-ocular fluid dynamics.

Dr. Grant's studies on the rate of aqueous humor outflow, correlated with the gonioscopic findings, have shown convincingly that the one common denominator in the various types of glaucoma is obstruction to outflow. In the "narrow angle" type it is intermittent and dependent on the closure of the angle by the iris whereas in the "wide angle" type it is continuous and dependent on changes inherent within the filtration structures.

The method of tonography developed by Dr. Grant has been based on the automatic recording of the rate of intra-ocular pressure and volume change during a 4-5 minute period of application of an electric tonometer on the intact eye.\* A simplified technique for making these tonographic measurements has now been found feasible when the automatic recording equipment is not obtainable. Also, a nomogram has been worked out to facilitate the interpretation of tonographic measurements for clinical use.

It is expected that tonography in the simplified form will be employed principally for the diagnosis of glaucoma. Experience with this method to date indicates that in cases where the distinction of glaucomatous from normal eyes is

\* For these studies Dr. Grant was awarded the first annual prize of the New England Ophthalmological Society for "the most valuable contribution made in ophthalmic science by a resident of New England during 1950."

uncertain by regular tonometry, a more reliable differentiation is obtainable by tonography. It appears that in addition to other advantages, tonographic diagnosis of glaucoma may be less subject to error from abnormalities of scleral rigidity than is regular tonometry.

As a laboratory correlate of the foregoing clinical studies, measurements have been made on the pressure-volume relationships in enucleated human eyes and in rabbit eyes. Studies have also been initiated on the aqueous humor flow in rabbits. For these studies a new type of pressure recording system has been devised, employing an electronic strain gauge and device for measuring minute volume changes. By this means it has been possible to obtain independent evaluation of the calibration data which are essential in tonography of the intact eyes of patients and to convert the measurements into realistic physical terms. This new and direct intra-ocular recording system has also been applied to tonometric measurements with rabbit eyes. This greatly facilitates the experimental study of pressure gradients within the eye and the determination of pharmacologic effects on aqueous humor flow.

## NEURO-OPHTHALMOLOGY

The fertile interdepartmental interest in matters pertaining to the neurology of the eye and visual mechanisms has resulted in the collection of an impressive amount of anatomic and clinical material illustrating neuro-ophthalmic mechanisms and aberrations. Dr. Donaldson has prepared and photographed unique dissections of the orbit, cranium, and brain illustrating the motor and sensory systems concerned with vision.\* At the same time Dr. Cogan has continued his collection of clinical case studies with the tentative aim of preparing a teaching atlas if the demand is sufficient and the resources are found. The material is currently being utilized in several postgraduate courses.

Of the numerous by-products emanating from the Howe Laboratory's interest in neurology of the eye, mention may be made of the unofficial supervision by Dr. Cogan of that

\* For his presentation of these stereophotographs, Dr. Donaldson was awarded Honorable Mention at the Exhibit of the American Medical Association, Section on Ophthalmology, Atlantic City, New Jersey, June, 1951.

portion of the house officer training program, the centralization of neuro-ophthalmic study cases, and the participation in experimental neuro-ophthalmic projects. Dr. Cogan was privileged to collaborate with Dr. Byron Waksman\* in an attempt to produce retrobulbar neuritis in rabbits by means of induced hypersensitization. Experiments aimed at obtaining an objective method of measuring visual acuity by the optokinetic response were conducted in the Howe Laboratory by Dr. Marvin Posner.† Also noteworthy is the clinical study by Dr. Herbert Giller‡ on ophthalmologic aspects of meningeal hydrops.

### RADIANT ENERGY

The studies on irradiation cataract, sponsored by the Atomic Energy Commission, have been pursued along direct and unexpectedly indirect lines. Studies on rabbits by Drs. Cogan and Donaldson have indicated that cataracts occur with doses as low as 250 r (1.2 m.e.v.) and comparable studies by Drs. Cogan, John Goff‡ and Elizabeth Graves‡ with neutrons show the threshold dose to be of the order of  $2 \times 10^9$  particles/cm.<sup>2</sup> incident on the lens. Moreover cataracts may be induced by irradiation without manifesting other abnormality in the eye. The susceptibility to cataracts was found to decline progressively throughout the life span of the animal.

Drs. Cogan, Donaldson, and Algernon Reese§ made a survey of all the material that could be collected bearing on irradiation cataracts in human beings. From this it was concluded that the pathogenesis of this type of irradiation cataract consisted in an inability of the lens epithelial cells to differentiate into fibers at the equator. Instead the aberrant cells migrated to the posterior pole of the lens where they underwent an abortive form of differentiation and opacification.

As a consequence of his conjoint interest in irradiation cataracts and stereophotography of the eye, Dr. Donaldson

\* Department of Experimental Neuropathology, Massachusetts General Hospital.

† House Officer, Massachusetts Eye and Ear Infirmary.

‡ Los Alamos Scientific Laboratory, Los Alamos, New Mexico.

§ Clinical Professor of Ophthalmology, College of Physicians and Surgeons, Columbia University, New York, New York.



was sent to Japan for a month under the auspices of the Atomic Energy Commission to make pictorial records representing various stages of cataract formation in atomic bomb survivors. Dr. Robert Sinskey, who is currently in Japan with the Atomic Bomb Casualty Commission, spent two training months in the Howe Laboratory prior to going overseas. As a further indirect result of the Laboratory's participation in studying irradiation cataracts, Dr. Donaldson is supervising the construction for the Atomic Energy Commission of several cameras to be assigned to government agencies concerned with the cataract problem. These cameras are being constructed in a machine shop set up by the Atomic Energy Commission and the Howe Laboratory.

### RETINITIS PIGMENTOSA

Through the interest and generosity of Mr. Chandler Hovey, it has been possible to set up a study on retinitis pigmentosa. Dr. Zeavin, in conjunction with Dr. George Wald,\* has built a "perimetric" dark adaptometer that permits light sensitivity measurements in areas within  $40^\circ$  of the point of fixation. By means of color filters it has been possible to determine the separate functional activity of rods and cones in different foci of the retina. Exploratory studies are being made with this apparatus in patients with retinitis pigmentosa, retinitis punctata albescens, and macular degeneration with the hope of obtaining a reliable index of effectivity for any therapeutic agent. A single case study using subconjunctival vitamin A aldehyde in the treatment of retinitis pigmentosa was disappointing.

### MISCELLANEOUS

Injury to the eye by a wide variety of substances has been casually tested by Dr. Grant. The agents tested have been mostly those encountered by chance in the Clinic and include the following motley collection: household detergents, shampoos, golf ball ingredients, bleaching solution, phenolic compounds, and calcium hydroxide.

Studies by Dr. Howard Blazar on corneal vascularization

\* Department of Biology, Harvard College.

have indicated that cortisone does not retard neovasculogenesis as had been hoped.

Studies on the clinical entity of Adie's pupil have been made by Drs. Marvin Posner and Grant. It was found that these pupils showed less hypersensitivity to pilocarpine than to mecholyl. Similarly cats which had prior removal of the ciliary ganglion also showed less sensitization to pilocarpine than to mecholyl. These observations are compatible with the current belief that the clinical and experimental conditions are allied phenomena.

The Howe Library continues effectively to serve a wide community of interests under the joint aegis of the Howe Laboratory and the Massachusetts Eye and Ear Infirmary. Mr. Charles Snyder became the librarian in April and has carried through the cataloguing, distributing, and advising functions of an active reference center. In addition he arranged a showing of motion picture films on various ophthalmological subjects for the residents' training course.

#### POLICY, ORGANIZATION AND FINANCES

The following letter to Dr. F. Stone is, in a sense, a synopsis of the Howe Laboratory's present position. Dr. Stone is Chief of the Extramural Programs of the new Institute for Neurologic Diseases and Blindness of the Public Health Service and the following letter is a reply to his request for comments on the current trends of ophthalmic research.

*December 15, 1951*

DR. FREDERICK L. STONE  
National Institute of Neurological Diseases  
and Blindness  
National Institutes of Health  
Bethesda 14, Maryland

DEAR DR. STONE:

I am happy to reply to your letter of December 3rd, as it pertains to a subject of deep personal concern. In fact, you may permit me to answer with specific reference to the Howe Laboratory, since that which applies to the Howe Laboratory applies, I believe, widely to ophthalmic research in this country.

During the past ten years we have attempted to bring basic scientists into ophthalmic fields of investigation encouraging them to apply their talents in a Laboratory which is closely associated with a clinic and in collaboration with clinicians. This is based on the belief that the accumulation of knowledge and diversification of techniques has become so vast that the individual investigator of the past must be replaced by a laboratory unit consisting of several individuals representing different fields. This collaboration has proved eminently successful in evolving new concepts of the basic operation of the eye and in making practical contributions to the understanding and treatment of ophthalmic disease.

There is every reason to think that this collaborative type of research will continue to be productive, so long as the basic scientist and clinical investigator can be offered the facilities and security for long-term studies. To expect a basic scientist to go into the sub-specialty of ophthalmic research as a serious career it is necessary to guarantee him the same academic security and resources as apply to other departments. Our problem, and I am sure it is a general one, is to maintain a respectable department with the shrinking buying power of income from our small endowment. The ready availability of short-term money for specific projects has not provided the substance for long-term planning of career investigators. Accordingly, we have had to drop one full-time appointment and are considering dropping another.

Investment in an established laboratory that has been shown to carry on ophthalmic research conscientiously and effectively would seem to me the proper participation of a Government agency, especially at a time when private sources of income are becoming less available. Those who have been close to the operation of basic research realize how much more promising is the investment in individuals than in types of problems. In fact, rigid specifications of the problem often subvert the whole purpose of the research. It may be hoped, therefore, that the emphasis in support of ophthalmic research will be on promising individuals and laboratories rather than on specific projects.

I hope these semi-philosophic remarks will be of service



to you in making out your program. While they do not answer some of your questions specifically, I believe they are pertinent for the trends in future research and new fields of exploration will depend largely on the individuals and the opportunities that become available. They cannot be determined in advance.

A survey of the desirable income based on the organization and operation of the Howe Laboratory was presented by V. Everett Kinsey several years ago and published in *Science* (Volume 105: pages 373-378, April, 1947). It was estimated that support of a research program such as we represent should be of the order of \$100,000 annually. Actually the fixed income has been of the order of \$32,000 with the addition of something less than an equivalent amount from solicitations.

Sincerely yours,

DAVID G. COGAN, M.D.

Finally it is with a great sense of satisfaction that the Howe Laboratory acknowledges the contributions of the following individuals and organizations that have materially helped in the balancing of the budget. To them and to many others who have contributed by other means we all have reason to be profoundly grateful.

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For studies on aqueous humor dynamics:

The Snyder Foundation

For studies on radiation cataracts:

Atomic Energy Commission

For studies on retinitis pigmentosa:

Mr. Chandler Hovey

DAVID G. COGAN, M.D.

*Director*

## PUBLICATIONS — 1951

COGAN, D. G.

Japan — after the bomb. Harvard Alumni Bulletin, January 13, 1951.  
Applied anatomy and physiology of the cornea. Symposium: Corneal Diseases. Tr. Am. Acad. Ophth. 329-406, March-April, 1951.

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Registry of interesting cases. Arch. Ophth. 45: 507, May, 1951.  
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GRANT, W. M.

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KINSEY, V. E.

The chemical composition and the osmotic pressure of the aqueous humor and plasma of the rabbit. J. Gen. Physiol. 34: 389-402, January 20, 1951.

## LECTURES — 1951

### COGAN, D. G.

- Round table discussion on miscellaneous ophthalmic problems. Eastern Section Meeting of the Association for Research in Ophthalmology, in New York City, New York, January 27, 1951.
- Cataract formation. Boston Society of Biologists, Symposium on the Effects of Irradiation on Cells, Harvard Medical School, in Boston, Massachusetts, February 21, 1951.
- Lesions of the posterior corneal surface. Buffalo Eye-Bank and Research Society, Inc., in Buffalo, New York, March 8, 1951.
- Lesions of the posterior corneal surface. Symposium on External Ocular Diseases, State University of Iowa, Iowa City, Iowa, March 21, 1951.
- Fundus in cardiovascular disease. Graduate Course in Cardiology, Massachusetts General Hospital, in Boston, Massachusetts, May 8, 1951.
- Fundus lesions in ophthalmology and external diseases of the eye. Postgraduate Course in Medicine, Massachusetts General Hospital, in Boston, Massachusetts, July 2 and 3, 1951.
- Effects of radiation on the eye. Medico-Military Symposium, United States Naval Hospital, in Chelsea, Massachusetts, October 31, 1951.
- and Donaldson, D. D. Symposium on Neuro-Ophthalmology, House Officers' Course, Massachusetts Eye and Ear Infirmary, December 27, 1951.
- House Officer Lectures.
  - Pathology of corneal disease. January 3, 1951.
  - Neuro-ophthalmology. February 2 and 9, 1951.
  - Lesions of the posterior corneal surface. February 28, 1951.
  - Anterior corneal lesions. June 4, 1951.

### DONALDSON, D. D.

- Radiation cataracts in experimental animals. Quarterly Meeting of Bio-Medical Program Directors, United States Atomic Energy Commission, in New York City, New York, February 21, 1951.
- Relationship of radiation cataracts in humans and experimental animals. Atomic Bomb Casualty Commission Medical Meeting in Hiroshima, Japan, May 1, 1951.

### GRANT, W. M.

- Clinical measurements of aqueous outflow. Section on Ophthalmology of the American Medical Association, Atlantic City, New Jersey, June 14, 1951.
- Clinical tonography. American Academy of Ophthalmology and Otolaryngology in Chicago, Illinois, October, 1951.





